SHORT REPORT

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Cytotoxic Constituents from the Rhizomes of *Monstera deliciosa*

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Abstract: A phytochemical study of the rhizomes of *Monstera deliciosa* has led to isolation of fourteen compounds (**1**-**14**) for the first time from the plant species. The structure elucidation was carried out using 1D and 2D NMR data. The cytotoxic activities of the compounds against the liver (HepG-2), larynx (Hep-2), colon (HCT-116), and breast (MCF-7) cancer cell lines were evaluated using MTT assay. Syringaresinol (**6**) showed remarkable IC_{50} values against the four tested cell lines. In addition, 9, 12, 13-trihydroxy-10-octadecenoic acid (**14**) was highly cytotoxic against Hep-2 and HCT-116 cell lines.

Keywords: *Monstera*; Araceae; cytotoxic; lignan.

1. Plant Source

Monstera deliciosa Liebm. whole plant was collected from Mansoura University, Mansoura, Egypt in July 2011, and the rhizomes of the species were separated from the rest of the plant. The plant was identified by Dr. Mahmoud Makram Kassem, Department of Vegetables and Ornamentals, Faculty of Agriculture, Mansoura University. A voucher specimen was deposited at the Department of botany and microbiology, Faculty of Science, Herbarium, Damietta University (DAM00022).

2. Previous Studies

In our previous *in vivo* study, the rhizomes of *M. deliciosa* exhibited significant antihyperglycemic effects in STZ-induced rats [1]. *In vitro* activity on the ethanol extract of the fruit of the species was shown to increase the insulin secretion [2]. Cytotoxic [3], anti-inflammatory, and wound healing activities of the extract of the leaves of the species were also reported in former studies. However, the extract of the leaves did not exhibit any antibacterial activity [4]. In addition to those activities, the *in vivo* anticancer and antioxidant activities of the methanol extract of the species were reported [5]. In contrast to the leaves of the species, the extract of stems was reported as an

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antibacterial agent together with antioxidant activity [2]. The simple phenolics, flavonoids, and tannins contents of the species were reported from the stem of the plant [2]. About 400 volatile constituents of the fruit of the species were reported by simultaneous steam distillation-solvent extraction and GC-MS [7].

3. Present Study

The different fractions of the methanol extract the rhizomes of *M. deliciosa* were subjected to chromatographic separation and purification leading to the isolation of 14 compounds for the first time from the plant. The present study deals with the isolation and identification of those compounds together with their *in vitro* cytotoxic activities against the liver (HepG-2), larynx (Hep-2), colon (HCT-116) and breast (MCF-7) cancer cell lines. The dried rhizomes (3 kg) of *M. deliciosa* were powdered and extracted by maceration with MeOH (6 x 5 L) at room temperature (20-25 ^{o}C). The filtered and dried extract (200 g) was partitioned with H_2O/petroleum ether and H_2O/CH_2Cl_2 to afford the petroleum ether (45.5 g) and methylene chloride (14.7g) fractions, respectively. The resulting fractions were subjected to normal (Silica Gel G 60-230, Merck, Germany) and reversed-phase chromatography (RP-C_{18}, Merck, Germany) as well as crystallization to afford compounds **2**, **4**, **5**, **9**, **10**, **11**, **12**, and **13** from the petroleum ether fraction and compounds **1**, **2**, **6**, **7**, **8**, and **14** from the methylene chloride fraction. Detailed purification steps are depicted in Figures S1-S4.

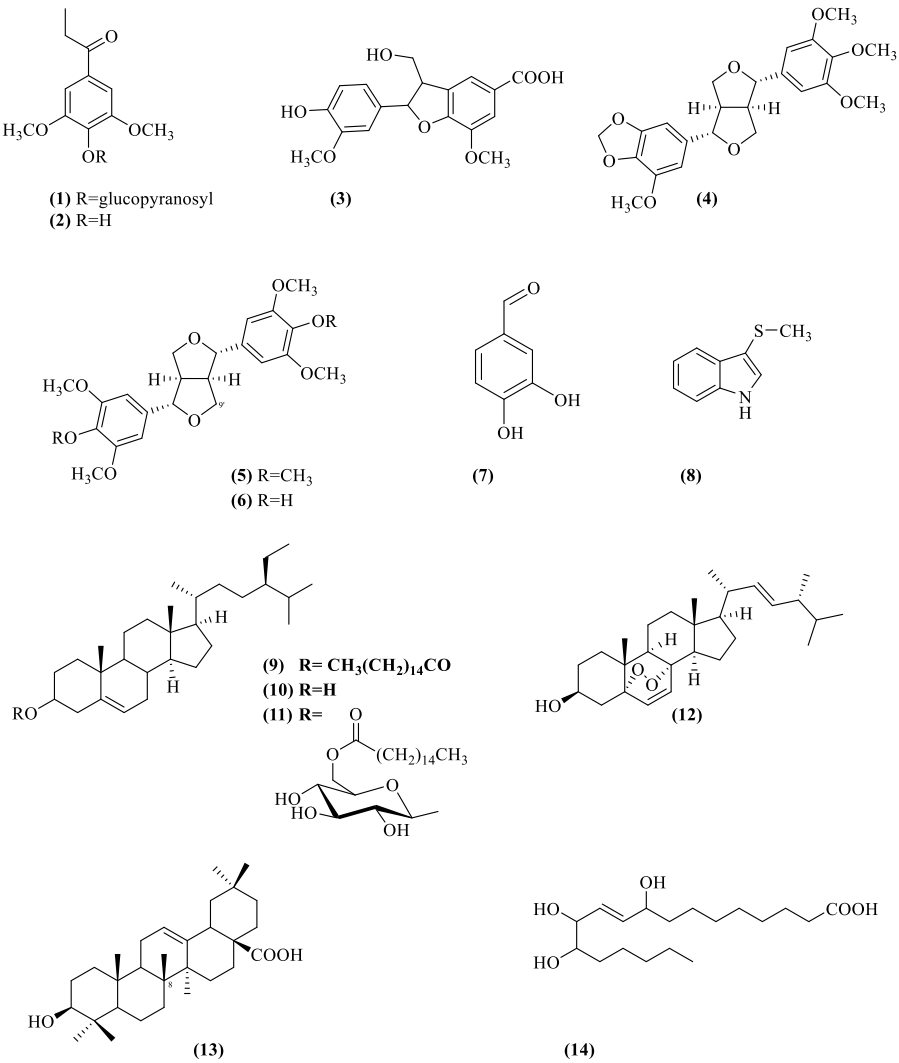

Figure 1. Structures of compounds (**1-14**) isolated from the rhizomes of *M. deliciosa*

Cytotoxic activity- MTT Assay: The assay was carried out according to Mauceri [8]. The cytotoxic activity was investigated against human cancer cell lines from the liver (HepG-2), larynx (Hep-2), colon (HCT-116), and breast (MCF-7) originated from ATCC (Manassas, VA, USA) and were obtained from VACSERA, Cairo, Egypt. The isolated compounds were dissolved in DMSO and diluted with PBS to concentrations of 400, 200, 100, 50, and 25µg/mL. In all experiments, control cells were dissolved with DMSO alone. A BioTeck® microplate reader (Winooski, VT, USA) was used to determine the optical densities. Statistical analysis of the data was performed using Microsoft Excel software version 2010.

Compounds **1**-**14** were isolated using a series of normal and reversed-phase chromatography as well as crystallization. The compounds were identified based on their NMR spectroscopic data (Figure 1). Their structures were confirmed by comparing their spectral data with those reported in the literature. They were identified as follows; propiosyringone-*β*-D-glucopyranoside (**1**) [9], propiosyringone (**2**) [10], ceplignan (**3**) [11], sesartemin (**4**) [12], yangambin (**5**) [12], syringaresinol (**6**) [13], protocatechuic aldehyde (**7**) [14], 3-methyl thio-indole (**8**) [15], *β*-sitostertyl palmitate (**9**) [16], *β*-sitosterol (**10**) [17], 7-oxo- *β*-sitosterol-3-*O*-*β*-D-glucopyranoside)-6'-palmitate (**11**) [18], 5α, 8α-*epi*-dioxyergosta-6, 22-dien-3*β*-ol (**12**) [19], oleanolic acid (**13**) [19], 9, 12, 13-trihydroxy-10-octadecenoic acid (**14**) [20]. This is the first report of compounds **1**-**14** from *M. deliciosa* (Figures S5-S39, Tables S1-S8).

The cytotoxic activities of compounds **1**-**14** were evaluated using an MTT assay against human cancer cell lines from the liver (HepG-2), larynx (Hep-2), colon (HCT-116), and breast (MCF-7) (Table 1 and see S1, in supporting information) [8]. For HepG-2 cells, compound **6** showed the highest cytotoxicity with an IC_{50} value (19.01 ± 0.16 µM) that is about a third of that of 5-Fu (IC_{50} = 62.57 ± 1.85 µM). Meanwhile, compounds **9** (IC_{50} = 31.53 ± 0.81 µM) and **14** (IC_{50} = 30.50 ± 0.43 µM) showed remarkable activity as about half the IC_{50} value of 5-FU. It is worth mentioning that *β*–sitosterol is reported to exert antihepatocellular cancer activity [21]. It was noticed that esterification with palmitate greatly enhanced the activity since compound **10** showed IC_{50} value of 55.55 ± 0.79 µM, which is still higher than 5-FU. All compounds showed comparable or higher cytotoxic activity on Hep-2 cells as compared to 5-FU (IC_{50} = 40.12 ± 0.62 µM) except for compound **8** (IC_{50} = 71.85 ± 1.32 µM) which was about half the potency of 5-FU.

Table 1. Cytotoxicity data of compounds **1**-**14** and 5-Fluorouracil (**5-FU**) against different cell lines using MTT assay as IC_{50} values

	***In vitro* Cytotoxicity IC_{50} (µM)**			
Compounds	**HepG2**	**Hep-2**	**HCT-116**	**MCF-7**
1	65.86 ± 2.02	24.64 ± 0.53	30.14 ± 0.64	66.34 ± 1.18
2	53.83 ± 0.94	23.7 ± 0.62	31.65 ± 0.46	55.88 ± 0.96
4	44.86 ± 0.9	18.16 ± 0.59	21.67 ± 0.78	64.44 ± 0.02
5	71.35 ± 2.03	41.18 ± 0.4	28.53 ± 0.25	71.98 ± 0.35
6	19.01 ± 0.16	10.3 ± 0.47	14.34 ± 0.46	16.59 ± 0.17
7	45.03 ± 2.19	29.68 ± 0.11	44.81 ± 0.85	45.82 ± 0.98
8	128.6 ± 3.81	71.85 ± 1.32	60.89 ± 0.37	122.8 ± 1.72
9	31.53 ± 0.81	39.3 ± 1.03	12.43 ± 0.62	32.2 ± 0.71
10	55.55 ± 0.79	23.24 ± 1.14	25.68 ± 1.63	53.91 ± 1.02
12	53.93 ± 0.81	19.87 ± 0.19	24.98 ± 0.87	48.36 ± 0.01
13	60.12 ± 1.18	23.66 ± 0.88	23.49 ± 0.88	66.06 ± 0.11
14	30.5 ± 0.43	11.38 ± 0.67	16.18 ± 0.58	28.88 ± 0.21
5-FU	62.57± 1.85	40.12 ± 0.62	48.04± 0.39	38.05± 1.22

Data are expressed as mean ± SD of three independent experiments, each done in triplicate.

While compounds **6** and **14** were the highest cytotoxic with IC_{50} values of 10.3 ± 0.47 and 11.38 ± 0.67 µM, respectively, about fourth that of 5-FU (IC_{50} = 40.12 ± 0.62 µM) against Hep-2 cells, the

compounds **10**, **13**, **2** and its glucoside **1** showed comparable activity with IC_{50} values of 10.3 ± 0.47, 23.66 ± 0.88, 23.7 ± 0.62 and 24.64 ± 0.53 μM, respectively, corresponding to about half of the IC_{50} value of 5-FU. Cytotoxicity properties of oleanolic acid (**13**) against Hep-2 cells are previously reported in the literature [22].

For HCT-116, compounds **9**, **6**, and **14** showed significant cytotoxic activities with IC_{50} values of 12.43 ± 0.62, 14.34 ± 0.46 and 16.18 ± 0.58 μM, respectively, as compared to 5-FU (IC_{50}= 48.04 ± 0.39 μM).

While compound **6** showed the highest cytotoxicity against MCF-7 cell line ((IC_{50} = 16.59 ± 0.17 μM) as compared to 5-FU (IC_{50} = 38.05 ± 1.22 μM), compounds **9** and **14** also exhibited remarkable activity against the cell line as 32.2 ± 0.71 and 28.88 ± 0.21 μM, respectively.

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Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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